Remarks

Claims 25-28 and 30-33 are pending in the application. Applicants have amended the claims to overcome the rejections under 35 U.S.C. §112. The Examiner is respectfully requested to reconsider and withdraw the rejections in view of the amendments and remarks contained herein.

Amendments to Claims

Applicants have amended claims 25, 31, and 32 in this Amendment D. In particular, the claims are amended to add the term "in vitro." Claim 32 has also been amended to remove typographical errors. No new matter has been added. Upon entry of this Amendment D, claims 25-28 and 30-33 will remain pending in the application.

Rejection under 35. U.S.C. §112, first paragraph

Claims 25-28 and 31-33 stand rejected under 35 U.S.C. §112, first paragraph, for not enabling one skilled in the art to practice the claimed invention without undue experimentation. This rejection is respectfully traversed in view of the amendments to claims 25, 31 and 32.

In order to be enabled under 35 U.S.C. §112, first paragraph, "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'." *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Questions of enablement are evaluated against the claimed subject matter and the first analytical step requires a determination of exactly what subject matter is encompassed by the claims. See, MPEP 2164.08. All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further, the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The Examiner has rejected the claims under 35 U.S.C. §112, first paragraph, stating "It would require undue experimentation beyond that taught in the instant specification to determine the unambiguous correlation between increases in mRNA expression and increases in polypeptide expression." However, the claimed invention is directed towards a carcinogenic assay based on levels or patterns of mRNA expression in cells following exposure. The claims

are not directed to polypeptide expression, thus a correlation between mRNA and polypeptide expression is unnecessary. Accordingly, it is respectfully submitted that one skilled in the art reading the specification would be able to practice the claimed invention without undue experimentation.

Applicants respectfully submit that the amended claims 25, 31 and 32 are enabled and request withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Rejection under 35 U.S.C. § 102(e)

Claims 25-28 and 31-33 stand rejected under 35 U.S.C. §102(e) as being anticipated by Ecker (U.S. Pat. No. 6,451,424). Reconsideration and withdrawal of the rejection is requested for the reasons set forth below.

Claim 25

In order to be anticipating, a prior art reference must teach each and every element of the claimed invention. (MPEP §2131.01) In the instant application, amended claim 25 is directed to a method for determining a level or pattern of a carcinogenesis biomarker (i.e., nucleic acid) in vitro. The method requires (a) incubating a marker nucleic acid molecule under conditions permitting specific nucleic acid hybridization; (b) permitting hybridization between the marker nucleic acid molecule and a complementary nucleic acid molecule obtained from a cell; and (c) detecting the level or pattern of the complementary nucleic acid.

The cited reference, Ecker (U.S. Patent No. 6,451,424) describes creating and comparing alternative transcript forms of genes using individual ESTs to determine at least one molecular interaction site among a set of mRNA molecules. Nothing in the reference teaches specific nucleic acid hybridization, use of the 280 and 488 nucleic acid sequence as a biomarker, or hybridization between either the 280 or 488 marker nucleic acid and complementary nucleic acid obtained from the same cell as required by claim 25. Although Ecker notes SEQ ID NO. 280 as having an alternative tandem poly(A) site in the 3'-UTR (Table 1), indicating that more than one RNA species of this gene exists, Ecker does not teach detection of the 280 biomarker to determine levels of carcinogenesis. Thus, it is respectfully submitted that the cited reference does not teach every element of claim 25. Accordingly, Applicants respectfully submit that

claim 25 is not anticipated by Ecker. Withdrawal of the rejection under 35 U.S.C. §102(e) is respectfully requested.

Claims 26-28

It is respectfully submitted that claims 26-28, which depend from and further limit claim 25, are not anticipated by Ecker for the reasons stated above with respect to claim 25. Reconsideration and withdrawal of the rejection is respectfully requested.

Claim 31

Independent claim 31 as amended herein is directed to a method for measuring the carcinogenicity of a composition. The method comprises (a) culturing a cell line in vitro; (b) exposing the cell line to a composition; and (c) determining the presence or absence of mRNA which substantially hybridizes to at least one nucleic acid sequence selected from the group consisting of SEQ NOS: 280, 384, and 488 and complements thereof.

The cited reference, Ecker, does not teach culturing a cell line in vitro; exposing the cell line to a composition; or hybridization of mRNA to marker nucleic acids SEQ ID NOS. 280, 384 and 488 or complements thereof. Accordingly, each and every limitation of claim 31 is not taught by the cited reference. Therefore, it is respectfully submitted that claim 31 is not anticipated by Ecker. Reconsideration and withdrawal of the rejection under 35 U.S.C. §102(e) is respectfully requested.

Claim 32

Independent claim 32 as amended is directed to a method for measuring the carcinogenicity of a composition. The method comprises (a) exposing a hepatocyte in vitro to the composition; and (b) detecting the presence or absence in the hepatocyte of mRNA which substantially hybridizes to at least one nucleic acid sequence selected from the group consisting of SEQ NOS: 280, 384, and 488 and complements thereof.

Nothing in the cited reference teaches the use of hepatocytes in any process. Further, the reference fails to teach exposing a hepatocyte in vitro to a composition; or detecting the presence or absence of mRNA in a hepatocyte as required by instant claim 32. Accordingly, it is

respectfully submitted that Ecker does not anticipate claim 32 as amended. Reconsideration and withdrawal of the rejection under 35 U.S.C. §102(e) is respectfully submitted.

Claim 33

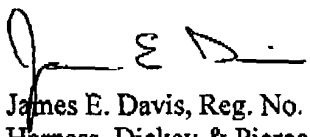
Claim 33, which depends from and further limits claim 32, is submitted as patentable over the cited reference for the reasons stated above with respect to claim 32. Reconsideration and withdrawal of the rejection are respectfully submitted.

Conclusion

It is believed that all of the stated grounds of rejection have been properly traversed or accommodated. Applicants therefore respectfully request that the Examiner reconsider and withdraw all presently outstanding rejections. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (314) 446-7683.

Applicants do not believe that any fee is required by the timely submission of this response. However, the Commissioner is hereby authorized to charge any required fees to Deposit Account No. 08-0750. Further, if there is any other fee deficiency or overpayment of any fees in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or credit such overpayment to Deposit Account No. 08-0750.

Respectfully submitted,



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Amendment D
U.S. Appl. 09/490,609
May 25, 2004

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Peggy Marie Leslie

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Amendment D (7 pages)
Fax Cover Sheet (1 page)